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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,852	09/22/2000	Per Johan Lundberg	A2200-IP US	1116

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EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1615	

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12/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/646,852	LUNDBERG ET AL.	
	Examiner	Art Unit	
	S. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10,12-18,20 and 23-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-10,12-18,20 and 23-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/05/09 has been entered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-10, 13, 16, 17, 20, 23-27 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Lundberg et al. WO 96/24338 A1.

Lundberg teaches an oral dosage form comprising: 1) a core that contains a proton pump inhibitor (PPI), one or more alkaline reacting compounds, and optionally pharmaceutical excipients; and 2) an enteric coating layer (abstract; page 19, lines 10-30; and examples). PPI includes omeprazole, it's salts, or it's enantiomer (claims 9-10). Pharmaceutical excipients include filler, binder, lubricant, surfactant, disintegrant, and other additives (page 12, lines 24-31). Example 3 discloses the use of sodium starch

glycolate (swelling agent) as one of the excipients. Alkaline reacting compounds include arginine, and alkali metal phosphate (page 10, lines 20-25). The core comprises starter seed such as sugar sphere (page 12, lines 15-22). Core can be in the form of tablet or pellet (page 9, lines 30 through page 10, lines 1-2; and page 13, lines 4-15). Enteric coating layer comprises a single polymer such as cellulose acetate phthalate, cellulose acetate succinate, or carboxymethylcellulose (page 11, lines 18-24). Enteric coating layer further comprises talc (examples).

It is noted that Lundberg teaches a separating layer between the core and the enteric coating layer. However, while the present claims recite that the core material is not coated with a separating layer, the claims do not preclude the coating of the swelling agent(s) as a layer between the active core and the semipermeable membrane. This is evident by the limitations recited in claims 6 and 20. Example 2 in the present specification further clarify the layers on the core include the swelling layer containing L-HPC. This layer is coated onto the PPI containing core before the semipermeable membrane. Moreover, the separating layer taught by Lundberg is formed by an in situ reaction between the enteric coating polymer and the alkaline core. The burden is shifted to the Applicant to show that the alkalizing additives and the semipermeable membrane of the present invention do not form an in situ separating layer. This is because the claimed dosage form utilizes the same alkaline reacting compound and the same polymer for the semipermeable membrane.

It is also noted that Lundberg does not teach that alkaline additives give a pH of not less than 8.5 when measured in a 2% w/w water solution/dispersion with a pH-

measuring electrode. However, such property is inherent because Lundberg teaches the use of the same alkaline additives.

Claim Rejections - 35 USC § 103

Claims 1, 3, 6-8, 12-18, 20 and 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Bergstrand et al. US 5,753,265.

Nara teaches a controlled release composition comprising a drug-containing core coated with a protective coating layer containing hydrophilic substances (column 6, lines 1-10). Hydrophilic substances include hydroxypropyl cellulose, hydroxypropylmethyl cellulose, methylcellulose, polyvinylpyrrolidone, and polyvinyl alcohol (column 5, lines 1-4). The amount of this protective coating is about 1 to about 15% to the core (ID). Drugs include omeprazole and lansoprazole (column 3, lines 59-60). The drug is mixed with excipient, such as sucrose or calcium phosphate (osmotic agent); binder; disintegrant, such as, sodium crosslinked carboxymethylcellulose or low-substitutional hydroxypropyl cellulose (swelling agent); and lubricant, including talc (alkaline additive) (column 5, lines 36-52; and examples). The core can be in the form of a granule, fine granule, or inert carrier particles including sucrose (column 5, lines 30-35, and 60-65). The coated core can be prepared in tablet or capsule form for oral administration (column 6, lines 56-65; and claim 7).

Nara does not explicitly teach the addition of a modifying agent in the protective coating composition.

Bergstrand teaches an omeprazole core is coated with a separating layer (protective coating layer) comprising polymer such as ethylcellulose, hydroxypropyl methylcellulose, polyvinylpyrrolidone, methylcellulose, and polyvinyl alcohol (column 7, lines 51-61). Bergstrand further teaches the polymer can be used alone (as a single polymer) (column 7, line 62). The separating layer further comprises plasticizer, and antistatic agents such as talc (column 7, lines 63-65; and examples 1, 3 and 7). Thus, it would have been obvious to one of ordinary skill in the art to modify the protective coating composition of Nara to include additives such as talc in view of the teaching of Bergstrand to obtain the claimed invention, because Bergstrand teaches adding talc to the coating composition to increase the thickness of the layer and thereby strengthen the diffusion barrier, because Bergstrand teaches the separating layer improves the chemical stability of the active substance and the physical properties of the dosage form (column 8, lines 21-27), because Nara teaches the desirability of using a separating layer to protect the acid sensitive active core, and because Nara teaches the use of other agent to help modify the coating properties (modifying agent) (example 11, lines 49-50).

Regarding the limitation “water-insoluble polymer capable of forming a semipermeable membrane”, it is noted that Nara and Bergstrand teach the use of the claimed water-insoluble polymers. Therefore, the burden is shifted to applicant to show that the water-insoluble polymers taught by Nara and Bergstrand do not have the claimed property. This is because identical chemical composition cannot have mutually

exclusive properties. A chemical composition and its properties are inseparable. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Bergstrand et al. US 5,753,265 and Hodges et al. US 5,225,202.

Nara is relied upon for the reason stated above. Nara does not explicitly teach the amount of alkaline additive present in the core.

Hodges teaches a controlled release pellet comprising acid labile drug in the core, and one or more buffering agents (alkaline additives) (see abstract, and column 3, lines 1-4; lines 15-19). Buffering agents present in the core in an amount ranging from about 1 to about 20% (column 3, lines 34-36). Thus, it would have been obvious to one of ordinary skill in the art to use alkaline additive in an amount taught by Hodges to obtain a stable acid labile composition, because Hodges teaches using buffering agent in an amount of about 1 to about 20% to aid in minimizing drug degradation in the core due to acid ingress in low pH environments (column 3, lines 6-9), and because Nara teaches a composition with low toxicity and can be safely used in mammals.

It is noted that Nara does not explicitly teach the weight ratio of the modifying agent to water-insoluble substance, as well as the amount of the alkaline additive and swelling agent in the core. However, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a

claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Thus, it would have been obvious to one of ordinary skill in the art to, by routine experimentation determine suitable amount of talc in the core composition as well as in the coating composition, because Nara teaches the release rate of the active ingredient is mainly in the small and large intestine without an enteric coating, while the release rate of the active ingredient is very limited in the stomach (column 1, lines 53-55; and column 7, lines 25-31), and because Nara teaches a coated formulation with low toxicity that can be safely used in human. The expected result would be a controlled-release composition comprising omeprazole in the core without enteric coating that can limit release of omeprazole in the stomach, but increases release in the small and large intestine.

Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Bergstrand et al. and, Zentner US 4,795,644 or Lundberg et al. 6,013,281.

Nara is relied upon for the reasons stated above. Nara is silent of the claimed alkaline agent.

Zentner teaches pH-modifying agent includes sodium mono- or di-phosphate (column 8, lines 3-15).

Lundberg teaches alkaline reacting compound includes arginine (column 6, lines 50-55). Thus, it would have been obvious to one of ordinary skill in the art to modify the

compositions of Nara using sodium mono- or di-phosphate and arginine compound as an alkaline agent, because the references teach suitable composition for the same active agent, namely, omeprazole, and because Nara teaches the desirability of using an alkaline agent in the composition.

Claims 4, 5 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Bergstrand et al., and Cotton et al. WO 98/54171.

Nara is relied upon for the reasons stated above. Nara is deficient in the fact that Nara does not specifically teach magnesium salt of omeprazole.

Cotton teaches novel form of S-enantiomer of omeprazole, including S-omeprazole, and more specifically, magnesium salt of S-omeprazole trihydrate (hereafter, the compound) (see abstract, and page 1, lines 4-10). Cotton also teaches the compound is formulated into oral dosage form, *e.g.*, capsule, tablet, and the like (page 6, lines 15-30). The formulation is effective as a gastric acid secretion inhibitor and is useful as an anti-ulcer agent (page 6, lines 1-14).

Cotton does not explicitly teaches the compound having a crystallinity of more than 70%, however, Cotton teaches that the compound of his invention is highly crystalline, *i.e.*, having a higher crystallinity than any other form of magnesium salt of S-omeprazole in the prior art (page 3, lines 24 through page 4, lines 1-7). Therefore, the burden is shifted to applicant to show the compound taught by Cotton does not have the crystallinity being claimed. It is also noted that Cotton teaches the trihydrate form, *e.g.*,

magnesium salt of S-omeprazole "trihydrate". However, applicant claims recite a generic form of magnesium salt of S-omeprazole with the transitional phrase "comprising of" permits any other form, including "trihydrate" taught by Cotton. Thus, it would have been obvious for one of ordinary skill in the art to modify the controlled release composition comprising a drug-containing core coated with a *non-enteric* coating composition using the magnesium salt of S-omeprazole trihydrate in view of the teaching of Cotton, because Cotton teaches the compound of his invention is more stable, easier to handle and store, easier to synthesize in a reproducible manner, because Cotton teaches the compound is most preferred in oral administration formulation, because Nara teaches a non-enteric coated formulation with low toxicity that can be safely used in human. The expected result would be a controlled-release composition comprising omeprazole in the core without enteric coating that can limit release of omeprazole in the stomach, but increases release in the small and large intestine.

Response to Arguments

Applicant's arguments filed 10/05/09 have been fully considered but they are not persuasive.

Applicant argues that the examiner determined that the separating layer of Nara *et al.* was equivalent to the single polymer composition of applicants' claims as a basis to maintain the obviousness rejection. *See* Sept. 4, 2008 Office Action, p. 10, lines 20-21. The examiner did not consider that the separating layer of Nara *et al.* is further

coated with the multi-polymer coating composition described in column 6, lines 15-21. Nowhere in Nara *et al.* does it teach coating a core material with only a separating layer or only a single polymer composition. Nonetheless, in response to the examiner's claim interpretation, applicants have amended the claims to state that "the core material is not coated with a separating layer." As explained above, express support for this recitation is located in the specification on page 3, lines 27-29 and in the examples. In view of the amendment, the rejection cannot stand because it does not account for a semipermeable membrane comprising a single polymer composition (wherein the single polymer composition is not a separating layer). Furthermore, as explained more fully below, there is no reason why one of skill in the art would modify the teachings of Nara *et al.* to exclude a separating layer and the multiple-polymer coating of Nara *et al.* (or the enteric coating of Bergstrand *et al.)*.

However, in response to applicant's argument that Nara fails to show certain features of applicant's invention, it is noted that the feature upon which applicant relies (i.e., the single polymer composition is not a separating layer) is not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, in response to applicant's arguments that *the separating layer of Nara et al. is further coated with the multi-polymer coating composition, and nowhere in Nara et al. does it teach coating a core material with only a separating layer or only a single polymer composition*, it is of note that the present claims do not preclude any coating layer outside or on top of the

semipermeable membrane. The "comprising" language in the preamble of the claims allow the present of other coating layer beyond the semipermeable layer, such as multi-layer coating composition.

Applicant argues that the cited references teach away from coating a core material with only a single polymer composition. Where a reference teaches away from and discourages a person skilled in the art from doing what is claimed, the reference established "the very antithesis of obviousness." In re Buehler 185 USPQ 781 (CCPA 1975). The prior art "must be considered in its entirety, including disclosures that teach away from the claims." MPEP § 2141.02(IV); see also, e.g., W.L. Gore &Associates, Inc. v. Garlock, Inc., 721 F.2d 1540 (Fed. Cir. 1983). The references cited in the rejection illustrate the "teaching away" in the art. These references teach that omeprazole should be coated with an enteric coating or by multiple polymers.

- Bergstrand et al. explains that H+K+-ATPase inhibitors such as omeprazole "are best protected from contact with acidic gastric juice by an enteric coating layer." See column 4, lines 5-7. It goes on to describe the inclusion of a separating layer in column 7, lines 43-50.
- Lundberg et al., U.S. Patent No. 6,013,281 ("Lundberg et al.") is directed to an enteric coated pharmaceutical dosage form of omeprazole. See, e.g., claim 3 and example 2. It also describes including a separating layer. See, e.g., the abstract.
- Hodges et al., U.S. Patent No. 5,225,202 ("Hodges et al.") is directed to an enteric coated pharmaceutical composition for a medicament that is sensitive to a low

pH environment. See the abstract. It describes using a "subcoat layer" to act as a physical barrier between the core and outer enteric coating layer in column 4, lines 59-65.

- Nara et al. is directed to a controlled-release composition formed by coating a core material with multiple polymers. See, e.g., the abstract. The specification lists examples of drugs that may be employed in the controlled-release composition in column 3, lines 34-64.

However, applicant's arguments are not persuasive for the following reasons:

1) the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Bergstrand is relied upon for the teachings of talc in a coating layer to reduce static.

2) as discussed above, the present claims do not preclude coating layers on top or outside the semipermeable membrane;

3) although Lundberg teaches a so called an "enteric" coating composition, said composition comprises the same single water-insoluble as claimed, namely, a cellulose esters;

4) with respect to the subcoat and/or separating layer, the Examiner notes that the swelling agents present in the core can be in the form of separating layer. See example 2 in the present specification; and

5) the separating layer of Nara comprises a single polymer.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 8:30 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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/S. Tran/
Primary Examiner, Art Unit 1615